Short Communication

Inhibitory Effect of Cholecystokinin Octapeptide on Vasoactive Intestinal Peptide-induced Stimulation of Adrenocortical Secretion

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Summary Vasoactive intestinal peptide (VIP) stimulated the pituitary-adrenocortical secretion following injection into the lateral ventricle of rats, but this effect was selectively inhibited by simultaneous administration of cholecystokinin octapeptide (CCK-8), but not by caeruletide.

Key Words: vasoactive intestinal peptide, cholecystokinin octapeptide, plasma corticosterone.

The occurrence of vasoactive intestinal peptide (VIP) in various structures of the central nervous system has been shown by a number of investigators. Immunoreactive VIP was also demonstrated in nerve endings of the hypothalamus (EMSON et al., 1978; BESSON et al., 1979) and in the hypothalamo-hypophyseal portal blood (SAID and PORTER, 1979). From these findings, VIP seems to be involved in the control of pituitary hormone secretion. Actually, several reports indicated that VIP stimulates the secretion of prolactin, affecting prolactin cells directly (SHAAR et al., 1979; ENJALBERT et al., 1980; ROTSZTEJN et al., 1980). Moreover, the release of growth hormone was shown to be influenced by VIP indirectly through the inhibition of somatostatin secretion (EPELBAUM et al., 1979; TAPIA-ARANCIBIA et al., 1980). As to the release of ACTH, we have observed that intracerebroventricular (i.c.v.) injection of VIP stimulates the pituitary-adrenocortical axis, but in vitro experiments showed that VIP could not cause the release of ACTH from the pituitary tissue (ITOH et al., 1982). We also found that cholecystokinin octapeptide (CCK-8) possesses a sedative action (KATSUURA and ITOH, 1982) and does not affect ACTH secretion when injected i.c.v. into rats (ITOH et al., 1982). Along the line of these observations, it would be of interest to examine the interaction of VIP and CCK-8 in regard to ACTH secretion.

Male Wistar rats, weighing 250–300 g, were housed at a constant temperature of 25°C under a controlled illumination of light/dark cycle, lights turned on
at 07:00 hr, with free access to standard rat biscuits and water. VIP (Peninsula Labs.), CCK-8 (Calbiochem.), and caeruletide diethylamine (Shionogi Res. Labs.) were dissolved and diluted with physiological saline just prior to use, and injected into the lateral ventricle of rats in a volume of 5 µl in the morning between 09:00 and 10:00 hr. Thirty min later the animals were decapitated and blood samples were collected. The method of i.c.v. injection was described in detail elsewhere (ITOH et al., 1979). Plasma corticosterone was determined by the method of ZENKER and BERNSTEIN (1958) with minor modifications. For statistical analysis of the data Student's t-test was used.

Our previous observation (ITOH et al., 1982) that i.c.v. injection of CCK-8 could not produce any increase in the plasma corticosterone level was confirmed in this study. Moreover, stress-induced elevation of plasma corticosterone was not affected by i.c.v. injection of CCK-8. The level under resting conditions was 12.3±2.69 µg/dl (S.E.M., n=10) and it increased to 43.8±2.69 µg/dl (n=14) after 30 min exposure to a strange environment in saline injected control group, and to 42.3±2.08 µg/dl (n=15) in rats injected with CCK-8 in a dose of 1 µg. As reported previously, i.c.v. injection of VIP produced dose-related elevation of the plasma corticosterone levels. When 1 µg of VIP was injected together with different doses of CCK-8, the effect of VIP was suppressed by CCK-8 dose-dependently (Fig. 1).

Next, the effect of caeruletide, which mimics many actions of CCK-8, was examined. The i.c.v. injection of this decapeptide in a dose of 1 µg produced a marked elevation of plasma corticosterone (31.4±2.28 µg/dl, n=14). When this amount of caeruletide was administered with 1 µg of VIP, the elevation of corticosterone level was not different from that after VIP alone (37.0±2.00 µg/dl, n=15).

Fig. 1. Effect of different doses of CCK-8 on VIP-induced elevation of plasma corticosterone. Plasma corticosterone was determined 30 min after i.c.v. injection of neuropeptides. ** P<0.01, *** P<0.001 vs. VIP alone.
CCK-8 ON ADRENOCORTICAL SECRETION BY VIP

This result indicates that central action of CCK-8 is not the same as that of caeruleptide, at least in its action of pituitary-adrenocortical stimulation. This might be due to the fact that caeruleptide is not a natural neuropeptide in the mammalian brain.

Corticotropin releasing factor (CRF) which stimulates the secretion of ACTH and β-endorphin was found by Vale et al. (1981), and CRF immunoreactivity was observed not only in the hypothalamus, but also in the thalamus, amygdala, cerebral cortex, midbrain, pons-medulla, cerebellum, and spinal cord (Olshowska et al., 1982). CRF was also shown to enhance behavioral effects of novelty (Britton et al., 1982), to decrease food intake and to produce a marked increase in grooming in rats (Morley and Levine, 1982). Although mechanisms and sites of behavioral actions of CRF are not yet known, central actions of various neuropeptides are now becoming the focus of psycho-neuroendocrinological investigations. Extensive studies of these neuropeptides are also carried out in relation to the secretion of pituitary hormones. The assumption that VIP stimulates CRF neurons in producing the release of ACTH may be related to the fact that i.c.v. injection of VIP induced a marked behavioral excitation (unpublished data). On the other hand, CCK-8 possesses sedative actions (Katsuura and Itoh, 1982). Thus, the actions of these two peptides are antagonistic in various respects. The present experiment indicated that when CCK-8 was administered centrally together with VIP, the stimulatory effect of the latter peptide on the ACTH secretion was apparently inhibited by CCK-8, but not by caeruleptide. Since stress-induced ACTH release was not affected by CCK-8, the suppressive action of this octapeptide is likely specific for VIP, and this effect seems to be due to its antagonistic action on VIP. The problem may be of particular importance, since both peptides are abundant in the cerebral cortex and assumed to be involved in the regulatory and integratory mechanisms of the cerebral functions.

REFERENCES


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